REMARKS

In response to the office action dated May 2, 2006, applicants have canceled claims 2 and 14, and have amended claim 1. Accordingly, claims 1 and 13 are under consideration. Applicants respectfully urge that the remarks set forth below will overcome the formal rejections and distinguish the claimed invention over the prior art of record.

Election/Restrictions

The office action acknowledges applicants' election of Group VIII, claims 1, 2, 13, and 14, without traverse, for further prosecution. Applicants confirm this election.

Specification objection

The examiner objected to an informality in the written description regarding the current priority status of the present application. Applicants have amended the written description to overcome this objection.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1, 2, 13, and 14 were rejected under 35 U.S.C. 112, first paragraph for allegedly failing to comply with the written description requirement. More specifically, the examiner states that the claims cover a genus of compounds that inhibit angiotensin II that were allegedly defined solely by its principal biological property. According to the examiner, the written description of the present application only reasonably conveys two species of angiotensin II inhibitors (i.e., losartan and enalapril) that reduce the progression or metastasis of a neoplasm. Therefore, the examiner concludes that the two species of angiotensin II inhibitors, but not the full breadth of the claims, satisfy the written description requirement.

Applicants respectfully disagree with the examiner's allegation that the genus of all angiotensin II inhibitors is not adequately described. Applicants respectfully direct the

examiner to page 5, first paragraph, of the office action, in which the examiner acknowledges that "a description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus..." Accordingly, applicants are not required to describe all the species within the genus of angiotensin II inhibitors to satisfy the written description requirement.

The claims have been amended so as to limit the angiotensin II inhibitor to an angiotensin II receptor type AT1 antagonist. Support for the limitation to AT1 antagonists is found in paragraph [0033], last three lines of the present application.

As a result of the amendment, the claimed genus is considerably smaller than it was in the original claim. In addition, a representative number of species of angiotensin II receptor type AT1 antagonists are provided, for example, in paragraphs [0033] and [0034] of the present application. Besides the two species mentioned by the examiner, the following species were also mentioned: Saralasin, Remikirin, BRL 36,378, CGS 14824, among others. Applicants respectfully submit that the written description provides a representative number of species of angiotensin II receptor type AT1 antagonists.

Next, claims 1, 2, 13, and 14 were rejected under 35 U.S.C. 112, first paragraph for allegedly not enabling a person having ordinary skill in the art to use the invention commensurate in scope with the claims. The original claim recited a method for reducing or preventing formation, progression, or metastasis of a neoplasm. The examiner has acknowledged that the specification is enabling for a method of reducing formation, progression, or metastasis of a neoplasm in a mammal. However, the examiner states that the specification does not reasonably provide enablement for a method of preventing formation, progression, or metastasis of a neoplasm in a mammal.

Applicants respectfully disagree that the written description lacks enablement for a method of prevention. However, merely to expedite prosecution, applicants have deleted the

term "or preventing" from the claims. Therefore, the specification enables the use of the invention commensurate in scope with the claims, as amended. Accordingly, the rejection is now moot and should be withdrawn.

Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112 be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §102(b)

Claims 1, 2, and 13 were rejected under 35 U.S.C. 102(b) for allegedly being anticipated by the Volpert et al. reference (referred to as "Olga et al." in the office action). According to the examiner, the Volpert et al. reference discloses that Captopril, an inhibitor of angiotensin converting enzyme, inhibits angiogenesis and reduces the growth of experimental tumors in rats. The examiner acknowledged that the Volpert et al. reference does not "explicitly teach administration of the angiotensin II antagonist to a human." See page 12 of the office action.

Applicants have limited the claims to treating humans. Support for the limitation can be found in the specification as originally filed, for example, on page 10, paragraph [0046]. As acknowledged by the examiner, the Volpert et al. reference does not disclose or suggest the treatment of humans. Therefore, the Volpert et al. reference cannot anticipate the present claims.

Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102 over the Volpert et al. reference be reconsidered and withdrawn.

Claims 1, 2, and 13 were rejected under 35 U.S.C. 102(b) for allegedly being anticipated by the Dudley et al. reference. According to the examiner, the Dudley et al. reference teaches that certain imidazole-pyridine derivatives are angiotensin II antagonists, useful for the treatment of brain cancer and other cancers.

The Dudley et al. reference, however, discloses that its method of treating neuronal tumors and other tumors depends upon the AT2 antagonizing properties of the angiotensin II antagonists and on the prevalence of AT2 receptors on the tumors. See column 4, lines 29 through 35, in which Dudley et al. states:

> [Imidazole-pyridine derivatives] by virtue of their AT2 antagonizing properties have utility in disrupting the function of tumor cells that contain AT2 receptors. Therefore, they are useful in blocking the actions and/or growth of neuronal tumors as well as other tumors wherein the AT2 receptor is prevalent (emphasis added).

The Dudley et al. reference lacks any disclosure of an effect of imidazole-pyridine derivatives on AT1 receptors in the treatment of tumors.

Applicants have limited the claims to administering an angiotensin II receptor type AT1 antagonist. As mentioned above, the Dudley et al. reference does not disclose or suggest the administration of an angiotensin II receptor type AT1 antagonist. Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102 over the Dudley et al. reference be reconsidered and withdrawn.

Claims 1, 2, 13, and 14 were rejected under 35 U.S.C. 102(b) for allegedly being anticipated by the Ashton et al. reference. According to the examiner, the Ashton et al. reference teaches a method of inhibiting the growth of neuronal tumor cells that contain AT2 receptors in a patient comprising administering an angiotensin II antagonist.

As with the Dudley et al. reference, and as acknowledged by the examiner, the Ashton et al. reference does not disclose or suggest the administration of an angiotensin II receptor type AT1 antagonist. Since the presently amended claims are limited to the administration of an angiotensin II receptor type AT1 antagonist, applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102 over the Ashton et al. reference be reconsidered and withdrawn.

Claims 1, 2, 13, and 14 were rejected under 35 U.S.C. 102(b) for allegedly being anticipated by the Griswold et al. reference (referred to as "Edgar et al." in the office action). According to the examiner the Griswold et al. reference "teaches a method of treating disorders such as tumor growth, i.e., neoplastic transformation and growth/metastasis (column 2, lines 6-12)."

Applicants respectfully disagree with the examiner's interpretation of the Griswold et al. reference. What the Griswold et al. reference teaches is the treatment of chronic inflammatory conditions. It is true that the reference at column 2, line 6-12 states the following:

> The observation of the presence of Angiotensin II receptors on synovial cells gives rise to the speculation that this tissue is reactive and proliferates in response to injury may reflect a broader role for angiotensin in the regulation of tissue injury, proliferation and differentiation. As such this would include treatment of disorders such as tumor growth, i.e., neoplastic transformation, and growth/metastasis, bone marrow maturation...(emphasis added).

However, it is incorrect that the Griswold et al. reference "teaches" a method of treating disorders such as tumor growth. The reference clearly states that the treatment of such disorders was mere "speculation." See column 2, line 6-12 of the reference.

The mere speculation that tumor growth in humans may be treated constitutes, at most, a suggestion to try. Such suggestions are insufficient to constitute a disclosure that renders a method recited in a patent claim unpatentable.

MPEP § 2145 repeats the admonition that it is "obvious to try" where "a new technology or general approach ... seemed to be a promising field of experimentation" See, *In re O'Farrell*, 853 F 2. 894, 903 (Fed. Cir. 1988).

As explained above, the Griswold et al. reference states a mere "speculation" for the treatment of disorders such as tumor growth (column 2, lines 6-12 of the Griswold et al. reference). This speculation constitutes no more than a potential promising field of experimentation, and meets the "obvious to try" standard of MPEP § 2145. Therefore, the Griswold et al. reference is an improper prior art reference in support of an obviousness rejection.

For the foregoing reasons, applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over the above-mentioned cited references be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §103 Over Volpert et al., in further view of Griswold et al.

Claim 14 was rejected under 35 U.S.C. § 103 as being unpatentable over the Volpert et al. reference in further view of the Griswold et al. reference. The examiner states that the Volpert et al. reference teaches that Captopril, an inhibitor of angiotensin converting enzyme (ACE), inhibits angiogenesis and slows the growth of experimental tumors in rats. The examiner concedes that the Volpert et al. reference fails to explicitly teach administration of the angiotensin II antagonist to a human.

To compensate for the deficiencies of the Volpert et al. reference, the examiner relies on the Griswold et al. reference. The examiner states that the Griswold et al. reference teaches a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist.

First, applicants have already overcome the Volpert et al. reference with respect to claim 1, from which claim 14 depends. Claim 14 has been cancelled, and the limitation of claim 14 has been incorporated into claim 1. Applicants have discussed above the reasons

why the Volpert et al. reference does not disclose the present invention. Therefore, the rejection of claim 14 is now moot.

Even if the rejection was not moot, there is insufficient motivation for a person having ordinary skill in the art to combine the teaching of the Volpert et al. reference with that of the Griswold et al. reference for at least two reasons.

First, these cited references teach the treatment of completely different conditions. As acknowledged by the examiner, the Volpert et al. reference teaches treating tumors in rats. In stark contrast, the Griswold et al. reference teaches the treatment of chronic inflammatory diseases in humans. Not only do the references disclose the treatment of different conditions, but they disclose the treatment of different organisms. Therefore, a person having ordinary skill in the art would not be motivated to combine these references.

Furthermore, as discussed above, the disclosure in the Griswold et al. reference regarding the treatment of tumors was pure speculation. Therefore, a person having ordinary skill in the art would not be motivated to combine the Volpert et al. reference with the Griswold et al. reference.

Second, the Volpert et al. and the Griswold et al. references teach completely different mechanisms of action regarding their respective angiotensin antagonists. The Volpert et al. reference teaches that the inhibition of endothelial cell migration was dependent on Captopril's inhibition of Zn^{2+}-dependent metalloproteinases. (See for example, page 671, right column, third paragraph).

The authors of the Volpert et al. reference considered Captopril's ability to inhibit ACE as a possible mechanism for the inhibition of cell migration. It is significant that the authors dismissed this possibility. See page 675, right column, second paragraph, which states:

> Angiotensin II, the product of ACE activity, can induce angiogenesis in vivo (17-20). Since cultured endothelial cells can contain the entire rennin angiotensin system (31), it was possible that captopril suppressed endothelial cell migration by inhibiting ACE. But this did not seem to be the case for several reasons.

See also Figure 5 in the Volpert et al. reference. Therefore, not only does the Volpert et al. reference not suggest the use of angiotensin II inhibitors, such as ACE inhibitors, the reference in fact teaches away from such use.

In stark contrast, the mechanism in which chronic inflammatory conditions are treated in Griswold et al. reference is through the inhibition of angiotensin II via angiotensin II receptor antagonists. See, for example, column 1, line 66 through column 2, line 5, in which it states:

> The present invention is a therapeutic method for treating chronic inflammatory conditions in a mammal, especially humans. The present invention has found that locally generated AII is present in human synovium and therefore use of AII receptor antagonists will contribute to the treatment of chronic inflammatory conditions.

Therefore, the mechanisms disclosed by these cited references are vastly different, and accordingly a person having ordinary skill in the art would not combine the Volpert et al. reference with the Griswold et al. reference for this second reason.

In conclusion, it is respectfully submitted that amended claim 1 and each of the claims dependent thereon are patentably distinguishable over the prior art.

Rejection Under 35 U.S.C. §103 Over Dudley et al., in further view of Griswold et al.

Claim 14 was also rejected under 35 U.S.C. § 103 as being unpatentable over the Dudley et al. reference in further view of the Griswold et al. reference. The examiner states that the Dudley et al. reference teaches imidazole-pyridine derivatives that are angiotensin II antagonists, and are useful for the treatment of cancers in which the AT2 receptor is prevalent. The examiner concedes that the Dudley et al. reference fails to explicitly teach administration of the angiotensin II antagonist to a human.

To compensate for the deficiencies of the Dudley et al. reference, the examiner relies on the Griswold et al. reference. The examiner states that the Griswold et al. reference teaches a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist.

First, applicants have already overcome the Dudley et al. reference with respect to claim 1, from which claim 14 depends. Claim 14 has been cancelled, and the limitation of claim 14 has been incorporated into claim 1. Applicants have discussed above the reasons why the Dudley et al. reference does not disclose the present invention. Therefore, the rejection of claim 14 is now moot.

Even if the rejection was not moot, there is insufficient motivation for a person having ordinary skill in the art to combine the teaching of the Dudley et al. reference with that of the Griswold et al. reference.

According to the examiner, the Dudley et al. reference teaches use of angiotensin II antagonists to treat memory loss and brain cancers and other cancers. As discussed above, however, the Griswold et al. reference teaches only treatment of chronic inflammatory conditions. The disclosure in the Griswold et al. reference regarding the treatment

of tumors was pure speculation. Therefore, the Griswold et al. reference cannot be said fairly to teach the treatment of tumors.

Accordingly, these cited references teach the treatment of completely different conditions. Therefore, a person having ordinary skill in the art would not be motivated to combine the Dudley et al. reference with the Griswold et al. reference.

In conclusion, it is respectfully submitted that amended claim 1 and each of the claims dependent thereon are patentably distinguishable over the prior art.

Double Patenting Rejection

The examiner rejected claims 1, 2, 13, and 14 for non-statutory double patenting over claims 1-3, 5-8, and 10 of U.S. Patent No. 6,641,811.

Applicants will address this rejection for non-statutory double patenting with terminal disclaimers, if appropriate, upon notification of patentable subject matter in the present application. The examiner is respectfully requested to withdraw, at least temporarily, this rejection for non-statutory double patenting until he indicates the presence of otherwise allowable subject matter.

In view of the foregoing amendments and remarks, entry of the amendments to the specification and favorable consideration of Claims 1 and 13 are respectfully requested. If the examiner has any questions or concerns regarding this amendment, he is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Anna C. Chau
Registration No.: 54,637

Agent for Applicant
HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(516) 822-3550
ACC/dlg
228867_1